Amendments to the Specification

The paragraph starting at line 18 on page 4 is amended as follows:

A commonly used prior art tool for illuminating electrophoretically separated gels is the ultraviolet transilluminator (light box). These light boxes, generally comprise a single wavelength set of ultraviolet producing fluorescent lamps. These lamps are generally horizontally mounted within the light box behind a window upon which the dye labeled sample rests. The window typically comprises an ultraviolet transmitting, ambient (visible) light blocking filter material. Other ultraviolet light boxes are commercially available that provide dual UV wavelength combinations of 254nm/365nm, 254nm/302nm and 365nm/302nm. In this regard, commercially available mid-range ultraviolet light boxes interchangeably use the wavelength designations 300nm, 302nm, 310nm or 312nm, since the UV bandwidth output of these wavelength designations is substantially the same. Additionally, UV light boxes are commercially available that provide all three UV wavelengths of 254nm, 302nm and 365nm. However, substantially all presently commercially available ultraviolet transilluminators (light boxes) use commercially available ultraviolet producing lamps that singly provide UV wavelengths in 365 ~~(UV-A) bandwidth~~ (UV-A bandwidth), 302nm

Amendments to the Specification continued

(UV-B bandwidth) and 254nm (UV-C bandwidth).

The paragraph starting at line 15 on page 5 is amended as follows:

Another device used to capture fluorescent labeled biological samples is commercially available from Bio-Rad, Inc. of Hercules, California under the name and style FLUOR S MULTIMAGER. This device uses a single broadband (290nm-365nm) ultraviolet fluorescent lamp. This ultraviolet fluorescent style tube lamp is horizontally mounted below the sample holding window and is typically scanned across the sample permitting the acquisition of the fluorescent signal via a charge coupled device (CCD) based camera system. This configuration limits the actual viewing of the fluorescent labeled sample by the researcher in real-time. The previously mentioned U.S. Patent No. 5,951,838 issued to Heffelfinger, et al. and entitled "Method and Apparatus for Correcting Illumination ~~Non-Uniformities~~ Non-Uniformities" describes this method in greater detail.

Amendments to the Specification continued

The paragraph starting at line 18 on page 7 is amended as follows:

The present invention provides a method and apparatus for use in genomic or proteomic research to visualize fluorescent labeled DNA, RNA or protein samples that have been separated for documentation and analysis. By way of summary, one form of the apparatus of the invention comprises a housing having interconnected ~~top bottom and side walls~~ top, bottom, and side walls defining an internal chamber and a sample supporting platform having a sample supporting area and radiation means disposed within the chamber for uniformly irradiating the sample supporting area with ultraviolet light at a first wavelength. The radiation means uniquely comprises a grid for emitting ultraviolet radiation constructed from a continuous, serpentine shaped ultraviolet tube that is strategically formed to provide a multiplicity of side-by-side, immediately adjacent irradiating segments. In one form of the invention the apparatus also includes a first conversion means that is removably carried by the housing at a location intermediate the radiation means and the sample supporting platform for converting the radiation emitted from said source of ultraviolet radiation to radiation at a second wavelength.

Amendments to the Specification continued

The paragraph starting at line 15 on page 8 is amended as follows:

With the foregoing in mind, it is an object of the present invention to provide a method and apparatus in which the uniformity of excitation radiation across the sample supporting surface of the apparatus is vastly improved when compared with the nonuniformity of radiation across the sample supporting surface of prior art transilluminators. More particularly, ~~if~~ it is an object of the invention to provide apparatus of the character described in which the Coefficient of Variation is well ~~about below~~ below about 5 to 10%.

The paragraph starting at line 6 on page 9 is amended as follows:

Another object of the invention is to provide a method and apparatus in which sequential analysis of several samples is greatly simplified and is substantially more accurate than is possible with prior art transilluminators because of the minimal effect on excitation intensity of sample positioning on the sample support surface. More particularly, ~~as~~ it is an object of the invention to provide a method and apparatus in which the same sample will give similar fluorescent intensities regardless of where the sample is ~~place~~ placed on the sample supporting surface of the apparatus.

Amendments to the Specification continued

The paragraph starting at line 5 on page 10 is amended as follows:

Figure 2 is a generally perspective, diagrammatic view illustrating ~~of~~ the non-uniform illumination of a sample supporting surface by a conventional, prior art transilluminator using a plurality of standard, [[side by side]] side-by-side fluorescent type UV lamps.

The paragraph starting at line 10 on page 11 is amended as follows:

Referring to the drawings and particularly to figure 1, one form of the apparatus of the invention for uniformly illuminating molecular samples with ultraviolet radiation is there shown ~~in~~ and generally designated by the numeral 12. The apparatus of this form of the invention comprises a housing 14 having interconnected top, bottom and sidewalls 16, 18, and 20 respectively that define an internal chamber 22. Carried by top wall 16 is a sample supporting platform 24 having a sample supporting area ~~of~~ or surface 26.

The paragraph starting at line 9 on page 12 is amended as follows:

By comparing the illumination pattern of a prior art transilluminator ~~is~~, as illustrated in figure 2 of the drawings, with the illumination pattern of the apparatus of the present invention as illustrated in figure 3 of the drawings, it is at

once apparent that the uniquely configured grid 30 of the apparatus of the present invention when combined with the conversion and dispersion means of the invention produces a vastly superior illumination of the sample supporting area than does the conventional transilluminator which embodies a plurality of standard, side-by-side fluorescent tubes.

The paragraph starting at line 17 on page 12 is amended as follows:

An important aspect of the apparatus of the present invention is the previously mentioned, first conversion means that it is carried by housing 14 at a location intermediate the radiation means, or grid 30, and the superimposed supporting surface 26 platform 24. This important first conversion means functions to convert the radiation emitted from the source of ultraviolet radiation, or grid 30, at a first wavelength of, for example 254 nanometers, to radiation at a second wavelength. This first wavelength conversion means here comprises a conversion plate 34 that is carried within the internal chamber of housing 14 at a location intermediate the sample supporting platform and the UV source 30. More particularly, plate 34 is provided with a conventional wave shifting phosphor coating 36. As is well known in the art, phosphors are compounds that are capable of emitting useful quantities of radiation in the visible and/or ultraviolet spectrums

Amendments to the Specification continued

upon excitation of the material by an external energy source. Due to this property, phosphor compounds have long been utilized in cathode ray tube (CRT) screens for televisions and similar devices. Typically, inorganic phosphor compounds include a ~~hose~~ host material doped with a small amount of an activator ion. In recent years, phosphor compounds, including phosphors in particular form, have been used in display devices, decorations, cathode ray tubes[[,]] and fluorescent lighting fixtures. Luminescence or light emission by phosphor particles may be stimulated by application of heat (thermo luminescence), light (photo luminescence), high energy radiation (e.g., x-rays or e-beams), or electric fields (Electro luminescence). A comprehensive discussion of various types of phosphors can be found in Patent No. 6,193,908 issued to Hampden-Smith et al.

The paragraph starting at line 18 on page 14 is amended as follows:

Also forming a part of the apparatus of this latest form of the invention is a reflector 41, which is carried by the bottom wall of housing 14. Superimposed over [[reflector-41]] reflector 41 is a second borosilicate plate 39a which is coated with a phosphor coating 37. With this construction grid 30 irradiates the phosphor coating on the ~~borosilicate~~ second borosilicate plate 39b converting the 254 nanometer radiation to 302 nanometers. The 302 nanometer radiation radiates

Amendments to the Specification continued

upwardly and downwardly, passes through the plate 39a and impinges upon reflector 41. Reflector 41 then reflects the radiation in an upwardly direction through plate 39 and upwardly of chamber 22. The reflected radiation is added to the radiation produced by the phosphor that coats the upper half of the segments of the grid, the upward radiation generated by means of plate ~~39b~~ 39a and all the combined radiation passes upwardly through filter 38 and impinges on the samples resting on the sample supporting or surface area 26.

The paragraph starting at line 18 on page 15 is amended as follows:

Positioned between the radiation means, or grid 30, and the sample supporting area 26 is a wavelength conversion means which is adapted to convert the UV radiation at the first wavelength of, for example, 254 nanometers to UV radiation at a second wavelength of, for example, 302 nanometers. This first wavelength conversion means here comprises a phosphor coating 37 disposed on the lower surface of a borosilicate plate 39 that is located between ~~in~~ the sample supporting area and the grid in the manner shown in figure 4A.

Amendments to the Specification continued

The paragraph starting at line 4 on page 17 is amended as follows:

Positioned between the radiation means, or grid 30, are first and second wavelength conversion means which are adapted to convert the UV radiation at the first wavelength of, for example, 254 nanometers to UV radiation at a second wavelength of, for example, 302 nanometers and then to UV radiation at a third wavelength of, for example, 365 nanometers. This first wavelength conversion means here comprises a first conversion plate ~~42~~ 40 that is carried by housing 14 at a location intermediate the sample support platform and the grid 30. In this instance, plate ~~42~~ 40 is provided with a wave shifting phosphor coating 43. The second wavelength conversion means of this latest form of the invention comprises a second conversion plate 44 that is also carried by housing 14 at a location between conversion plate ~~42~~ 40 and sample supporting platform 24. Plate 44 is provided with a wave shifting phosphor coating 46. It is to be understood that, with the construction shown in figure 6, either or both plates 40 and 44 can be removed from the housing and replaced with alternates plates if desired.

The paragraph starting at line 4 on page 18 is amended as follows:

As illustrated in figure 7 of the drawings, the UV source once again comprises the uniquely configured grid 30 that emits UV radiation at a first

wavelength of, for example, 254 nanometers. Positioned between grid 30 and the sample-supporting platform 24 is the novel previously mentioned dispersion means, here comprising a quartz fibrous mesh 50. This novel dispersion means, or fibrous mesh 50, functions to uniformly disperse the radiation generated by grid 30 in a manner to significantly contribute to the uniform illumination of the sample supporting platform 24. Disposed intermediate the dispersion means and the sample supporting platform 24 is a first wavelength conversion means, or conversion plate 34, that is carried within the internal chamber of housing 14 at a location intermediate the sample supporting platform <u>and</u> the fibrous mesh 50. More particularly, plate 34, which is of the character previously described, is adapted to convert the UV radiation at the first wavelength of about 254 nanometers to UV radiation at a second wavelength.

<u>The paragraph starting at line 18 on page 18 is amended as follows</u>:

Turning once again to figure 2, this drawing comprises a graphical representation of the nonuniform illumination of the sample supporting platform which results from ultraviolet radiation emitted from a conventional transilluminator having six side-by-side, elongated tubular shaped lamp radiation sources (distances along the left and backside of the sample supporting platform

are represented by the X and ~~y~~ Y axes in figure 2, while radiation intensity is represented by the Z axis). The data shown in figure 2 was obtained using a bench top transilluminator manufactured and sold by UVP, Inc., of Upland, California under the model designation M26X. This transilluminator uses six F8T5 302nm 8-watt lamps and embodies a 25cm x 26cm UV transmitting, ambient (visible light) blocking filter.

The paragraph starting at line 9 on page 19 is amended as follows:

The data represented in figure 2 was obtained by measuring the intensity of the 302nm radiation emitted by the ultraviolet lamps at 100 equally spaced (one inch apart) points 1.5 mm ~~form~~ from the filter surface (see Figure 8). The sensor used was a UVP, Inc. Model UVX-31 radiometer. The sensor was placed on each of the 100 points for 5 seconds and the intensity was recorded. The intensity of 185nm radiation emitted by the lamps was measured in the center of the filter at a location 2 mm above the surface. The sensor used was a sensor that is commercially available from International Light of Newbury Port, MA under the model designation IL1700. In this instance the sensor was outfitted with a model SEE220 sensor head. This latter measurement was used to estimate the relative levels of ozone production.

Amendments to the Specification continued

The paragraph starting at line 20 on page 19 is amended as follows:

As clearly shown in figure 2, the radiation intensity falls off markedly from the center of the sample supporting surface to the edges thereof. In the prior art of transilluminating[[,]] the excitation light intensity is thus dependent on position of the sample on the sample-supporting platform, making quantitative side-by-side and sequential comparisons extremely difficult. Accordingly, the same sample will give very different fluorescent intensities depending on where the sample is placed on the sample-supporting platform of the typical prior art transilluminator.

The paragraph starting at line 7 on page 20 is amended as follows:

Figure 3 comprises a graphical representation of the substantially uniform illumination of the sample-supporting platform of the present invention, which results from ultraviolet radiation emitted from the uniquely configured radiation sources, or grid 30, of the apparatus. Figure 3 clearly illustrates the dramatic improvement in the uniformity of excitation radiation across the sample supporting surface area 26 of the apparatus of the present invention when compared with the nonuniformity of radiation across the sample-supporting surface of the prior art transilluminator. With the coefficient of variation of (CV well below about 5 to

Amendments to the Specification continued

10% as illustrated in figure 3, meaningful, quantitative [[side by side]] side-by-side comparisons are quite possible using the apparatus of the present invention. In addition, sequential analysis of several samples is also simplified and is substantially more accurate because of the minimal effect sample placement ~~has position~~ position has on excitation intensity. Stated another way, the sample will give substantially similar fluorescent intensities regardless of where the sample is ~~position~~ positioned on the sample-supporting platform of the apparatus of the present invention.

Amendments to the Specification continued

The paragraph starting at line 9 on page 21 is amended as follows:

In obtaining the data used to plot the graphical representations shown in figures 2 and 3, the average intensity was calculated using the following formula:

$$\text{Output} = \frac{\sum_{i=1}^{n} X_i}{n}$$

The percent uniformity is the average of the row and column uniformity. This uniformity was calculated using the following formula:

Row uniformity=1-the tolerance of the row test point ~~divide~~ divided by the mean of the row test points (10)

Column uniformity=1-the tolerance of the column test point divided by the mean of the column test points (10)

Thus:

$$\text{Uniformity} = 1 - \frac{\max - \min}{\overline{X}},$$

$$\overline{X} = \frac{\sum_{i=1}^{n} X_i}{n}$$

The Coefficient of Variation (CV) is the standard deviation of the individual data points divided by the average. More specifically, the CV is a relative

measure of variation and independent of units, and is ideal for evaluating results from different experiments that use the same basic test or instrument. In this case, variations of the transillumination intensity across various transilluminator designs were quantified and compared. The lower the CV, the smaller the variation of intensity across the active area of the transilluminator.

$$\text{Coefficient of Variation} = \frac{s}{\overline{X}}$$

$$s = \sqrt{\frac{\sum_{i=1}^{n}(X_i - \overline{X})^2}{n-1}}$$

$$\overline{X} = \frac{\sum_{i=1}^{n}\overline{X}_i}{n}$$

It is to be noted that the Coefficient of Variation times $100 =$ percentage.

A study of figures 2 and 3 clearly demonstrates the value of the present invention and the substantial advancement over the prior art that it represents.

Having now described the invention in detail in accordance with the requirements of the patent statutes, those skilled in this art will have no difficulty in making changes and modifications in the individual parts or their relative assembly in order to meet specific requirements or conditions. Such changes and modifications may be made without departing from the scope and spirit of the invention, as set forth in the following claims.